UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency Office of Pesticide Programs

MEMORANDUM

6/26/2017

SUBJECT: Acute Toxicity Review for **Smartcel Sensitive,** EPA Reg. No.: **92916-R**

FROM: Narayanan Parthasarathy
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Product Science Branch
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THRU: Jenny Tao, Senior Scientist
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TO: Seiichi Murasaki, PM Team 33 / Aline Heffernan
Regulatory Management Branch I
Antimicrobials Division (7510P)

Registrant: **Smartfiber AG**		
Decision No.: **526677**	Submission No.: **999301**	E-Sub No.: **17473**
DP No.: **438679**	Action Code: **A540**	
MRID No(s).: **50190003-50190005**		

Formulation from label			
PC code(s)	CAS #(s)	Active Ingredient(s)	% weight
088502	1341-13-2	Zinc Oxide	16.0%
		Other Ingredients	84.0%
		Total	100.0%

I. BACKGROUND

On behalf of the **Registrant, Smartfiber AG,** the Consultant, **Wagner Regulatory Associates** has submitted an application for pesticide registration for their product: ***Smartcel Sensitive*, EPA Reg. No. 92916-R.** This antimicrobial zinc oxide fiber is formulated as an end-use product. It is intended for use in the manufacture of products (Textiles, Fabric, Wool, Cotton, Resins etc) to impart antimicrobial properties.

II. RELEVANT DOCUMENTS

	RECEIVED	N/A
EPA FORM 8570-35 – Data Matrix (2/16/2017)	☒	☐
Cover letter (2/17/2017)	☒	☐
Transmittal document	☒	☐
Basic CSF, (2/16/2017)	☒	☐
Proposed label	☒	☐
Acute Oral Toxicity Study (OSCPP 870.1100)	☒	☐
Acute Dermal Toxicity Study (OSCPP 870.1200)	☒	☐
Acute Inhalation Toxicity Study (OSCPP 870.1300) Waiver request	☒	☐
Primary Eye Irritation Study (OSCPP 870.2400) Waiver request	☒	☐
Primary Skin Irritation Study (OSCPP 870.2500)	☒	☐
Dermal Sensitization Study (OSCPP 870.2600) Waiver Request	☒	☐
Comments**:**		

III. FINDINGS/RECOMMENDATIONS

1) The registrant had provided studies to address Acute Oral and Acute Dermal toxicity and Primary Skin Irritation (MRID Nos 50190004, 650190003 & 50190007, respectively). The submitted studies are acceptable. A review of each study is attached to this memorandum.
2) **Acute Inhalation Toxicity:** The registrant is requesting **waiver** (MRID #5019005) and is acceptable based on the following rationale:

   The product is a solid fibrous material and a low-volatility product. The product could not be milled (see e-mail dated 5/9/2017) and the lab indicated that "it had worked with this product to conduct the afore-mentioned toxicity studies and based on that experience they predict the product material will not grind to respirable particles." In summary, the product could not be aerosolized.

3) **Primary Eye Irritation:** The registrant is requesting **waiver** (MRID #5019005) and is acceptable based on the rationale of inability to generate particles that could be retained in eyes upon exposure.
4) **Waivers mentioned above:** Please refer to OPP Guidance for Waiving or Bridging of Mammalian Acute Toxicity Tests for Pesticides and Pesticide Products (Acute Oral, Acute Dermal, Acute Inhalation, Primary Eye, Primary Dermal, and Dermal Sensitization - March 1, 2012).
5) **Skin Sensitization:** The registrant is requesting **waiver (MRID #5019006)** based on **RED.**

The acute toxicity profile of EPA Reg. No. 92916-R is currently

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	50190004	IV	Acceptable
Acute Dermal Toxicity	50190003	IV	Acceptable
Acute Inhalation Toxicity	50190005	Waived	Acceptable
Primary Eye Irritation	50190005	Waived	Acceptable
Primary Skin Irritation	50190007	IV	Acceptable
Dermal Sensitization	50190006	Waived	Acceptable

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V. PRODUCT LABELING

Based on the above acute toxicity profile, no specific **First Aid or human-hazard precautionary statements (or headings)** are required on the ***Smartcel Sensitive*** label except the front-panel statement **"Keep Out of Reach of Children" (KOROC).** The Agency PM may, in accordance with 40 CFR §156.66, decide whether to waive the KOROC requirement, and whether to approve its placement on other than the front panel.

The presence of the **signal word is optional.** If one is used, it must be **"CAUTION".**

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

(Up-And-Down Procedure in Rats)

Product Manager: Seiichi Murasaki RM 33/ Aline Heffernan **Reviewer:** N. Parthasarathy

MRID No: 50190004 **Study Completion Date:** 10/25/2016

Laboratory Study No: 42900

Testing Laboratory: Product Safety Labs
Author(s): Jennifer Durando, BS

Quality Assurance (40 CFR § 160.12): Included

Test Material: *Smartcel Sensitive*. Whitish Solid fibers. Expected to be stable for the duration of testing.

Species: Albino Rat; Sprague-Dawley.
Weight: 159-188g (Females)
Age: 9-10 weeks
Source: SAGE Labs
Housing: Temperature Range: 19 -23°C
Humidity Range: 40-57%
Photoperiod: 12- hour light/dark cycle
Acclimation: 8 or 15 days

Summary:

1. **LD_{50}:** >5000 mg/kg b.w.
2. **Tox. Category: IV**
3. **Classification:** Acceptable

Procedure (Deviations from 870.1100): The test substance was incorporated into peanut butter and administered as a test diet, instead of via oral gavage, due to the physical properties of the test substance. **Test Procedure:** The physical properties of the test substance prevented it from being administered by oral gavage; therefore, the test substance was incorporated into peanut butter and administered as a test diet. "A total mixture of 10 grams of the appropriate quantity (calculated based on animals' initial body weight) of the test substance and peanut butter were mixed together." The test diets were administered to the animals in "standard feeding jars" for an approximate 24-hour period. An initial limit dose of 5000mg/kg was administered into one animal. Due to the absence of mortality in this animal, two additional animals received the same dose. One of these animals died, not related to toxicity, within one day of exposure. One additional animal was tested. The animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily thereafter for 14 days.
Results:

Dosage (mg/kg)	Number Deaths/Number Tested		
	Males	Females	Combined
5000	-	3/4	-

Observations: The entire test substance diet was consumed by all animals**.** All animals survived exposure to the test substance and gained body weight, and appeared active during the study. No signs of gross toxicity, adverse clinical effects, or abnormal behavior. The animal that died exhibited reduced fecal volume prior to death.

Gross Necropsy: No gross abnormalities were noted for any of the animals when necropsied at the end of the 14-day observation period.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§ 81-2, 870.1200)

Product Manager: Seiichi Murasaki RM 33/ Aline Heffernan **Reviewer:** N. Parthasarathy

MRID No: 50190003 **Study Completion Date:** 8/4/2016

Laboratory Study No: 42901

Testing Laboratory: Product Safety Labs
Author(s): Jennifer Durando, BS

Quality Assurance (40 CFR § 160.12): Included

Test Material: *Smartcel Sensitive.* Whitish Solid fibers. Expected to be stable for the duration of testing.

Species: Albino Rat; Sprague-Dawley.
Weight: 203-250g (Females) 275-327g (males)
Age: 9-10 weeks
Source: SAGE Labs
Housing: Temperature Range: 19 -23°C
Humidity Range: 45-64%
Photoperiod: 12- hour light/dark cycle
Acclimation: 15 days

Procedure (Deviations from §81.2): None

Summary:

1. **Combined LD_{50}: > 5000 mg/kg b.w.**
2. **Tox. Category:** IV
3. **Classification:** Acceptable

Procedure (Deviations from 870.1200): None

Test Procedure: All animals were treated with 5000 mg test substance which was topically applied. The test substance was moistened with 0.5 ml distilled water before application. The animals were observed for mortality, signs of gross toxicity, and behavioral changes at least three times on the day of dosing and at least once daily for 14 days after dosing.

Results:

Dosage (mg/kg)	Number Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: No signs of gross toxicity, adverse clinical effects, or abnormal behavior.

Gross Necropsy findings: No gross abnormalities.

DATA REVIEW FOR PRIMARY SKIN IRRITATION TESTING (§ 81-5, 870.2500)

Product Manager: Seiichi Murasaki RM 33/ Aline Heffernan **Reviewer:** N. Parthasarathy

MRID No: 50190007 **Study Completion Date:** 8/4/2016

Laboratory Study No: 42902

Testing Laboratory: Product Safety Labs
Author(s): Jennifer Durando, BS

Quality Assurance (40 CFR § 160.12): Included

Test Material: *Smartcel Sensitive.* Whitish Solid fibers. Expected to be stable for the duration of testing.

Species: Rabbit/New Zealand White.
Weight:2484-2696g (Females)
Age: 14 weeks
Source: Robinson Services Inc
Housing: Temperature Range: 19 -22°C
Humidity Range: 38-48%
Photoperiod: 12- hour light/dark cycle
Acclimation: 15 days

Summary:
1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Procedure (Deviations from 870.2500): None.

Test Procedure: 0.5g of test substance was applied as a skin patch. Sufficient water to damp the material was used to ensure good contact with the skin. After 4-hour exposure, test sites were evaluated for erythema and edema formation at 30-60 minutes, 24, 48, 72 hours. Primary Dermal Irritation score was obtained by adding the average erythema and edema sores for 30-60 minute, 24, 48, and 72-hour soring intervals dividing by the number of evaluation intervals Evaluation was carried out using Draize score.

Results:

Time After Patch Removal	Erythema	Edema
30-60 min	2/3	0/3
24 hrs	1/3	0/3
48 hrs	0/3	0/3
72 hrs	0/3	0/3

Time After Patch Removal	Severity of Irritation – Mean Score
30-60 min	0.7
24 hrs	0.3
48 hrs	0.0
72 hrs	0.0

Conclusion: The Primary Dermal Irritation Index (PDII) = 0.3; Slightly Irritating.

Primary Dermal Irritation Index (PDII) Classification

PDII	Classification
0	**Non-irritating**
>0-2.0	**Slightly irritating**
2.1-5.0	**Moderately irritating**
>5.0	**Severely irritating**